Reproductive Tissue
FDA's Regulatory Framework

Jill Hartzler Warner, J.D.
Center for Biologics
Evaluation and Research,
Food and Drug Administration

Workshop on Evidence Based Assisted Reproductive Technologies

September 18, 2002

FDA's Statutory Authorities

- Public Health Service Act, Section 351
  - Biological products
- Federal Food, Drug, and Cosmetic Act, Section 201 et seq.
  - Drugs (including biological products) and devices
- Public Health Service Act, Section 361
  - Communicable disease

FDA's Proposed Approach

- Announced February 1997
- Selected as a Reinventing Government Report pursuant to the Vice President's National Performance Review
- Broad scope of human cells, tissues, and cellular and tissue-based products
- Implemented through rulemaking

Risk-based Approach First Tier

- Regulated solely under sec. 361 of PHS Act with focus on preventing transmission of communicable disease if:
  - minimally manipulated
  - labeled and advertised for homologous use
  - not combined with a drug or device
  - no systemic effect (some exceptions)

Risk-based Approach Second Tier

- Do not meet criteria
- Raise more significant clinical safety and effectiveness concerns
- Regulated as drugs, biological products, or devices
- Must still follow sec. 361 requirements

Proposed Approach -- Reproductive Tissue

- All reproductive tissue would be subject to controls aimed at preventing the spread of communicable disease
  - Authority derived from sec. 361 of the PHS Act
  - Registration of establishments
  - Donor screening and testing
  - "Good tissue practice"
  - Labeling controls, inspection, and enforcement

Proposed Approach -- Reproductive Tissue

- Additional requirements for "more than minimally manipulated" reproductive tissue
  - Authority derived from section 351 of the PHS Act
  - Regulation as biological product
  - Focus on demonstrating safety and effectiveness

Status of Rulemaking

- Final rule, "Human Cells,Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing," published January 2001
- Proposed rule, "Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement," published January 2001
- Proposed rule, "Suitability Determination for Donors of Human Cellular and Tissue-Based Products," published September 1999

FDA Correspondence Cloning Technology

- March 2001 “Dear Colleague” letter
- “FDA has jurisdiction over clinical research using cloning technology to clone a human being”
- Investigational new drug application (IND) required
- Due to major, unresolved safety questions, FDA would not permit clinical investigation to proceed at this time.

FDA Correspondence Genetic Transfer

- July 2001-- Letter to sponsor/researchers
- “FDA has jurisdiction over human cells used in therapy involving the transfer of genetic material by means other than the union of gamete nuclei”
- Examples: transfer of cell nuclei (including oocyte nuclei), ooplasm, genetic material contained in a vector
- INDs required

FDA Correspondence Co-Culture of Embryos

- March 2002 "Dear Colleague" letter
- "FDA has jurisdiction over human cells or tissues intended for transplant into a human recipient that have ex-vivo contact with live nonhuman animal cells, tissues, or organs."
- Examples: bovine tubal cells, Vero cells used for co-culture with human embryos
- INDs required

Investigational New Drug Application

- 21 CFR Part 312
- Applies to clinical investigations of drugs and biological products
- Submitted to FDA before clinical investigations begin
- 30 days must elapse before administration to humans
- Applies regardless of federal funding

IND: Principles

- Assure safety and rights of subjects
- Encourage innovation by allowing maximum flexibility in early research
- Assure quality of study design (Phases 2 and 3) to permit evaluation of effectiveness and safety
- Maximize efficiency of BLA review by promoting early consultation

IND: Principles

- Amount/type of information submitted depends on:
  - Novelty of biological product
  - Extent to which it has been studied previously
  - Known or suspected risks
  - Developmental phase of the product
  - Scope and nature of proposed protocols

IND: Process

- Sponsor responsibilities:
  - Select qualified investigators and oversee their conduct
  - Ensure compliance with protocols
  - Submit adverse experience reports and annual reports
  - Form FDA-1571

IND Process

- Investigator responsibilities:
  - Ensure study accords with protocol
  - Obtain informed consent from subjects
    - 21 CFR Part 50
  - Ensure investigational review board review and approval
    - 21 CFR Part 56
  - Form FDA 1572

Additional Resources

- Tissues
  - www.fda.gov/cber/tiss.htm
- Guidance for IRBs and Clinical Investigators
  - www.fda.gov/oc/ohrt/irbs